REMARKS

The first rejection of claims under 35 USC §112, first paragraph

Claims 44 and 90 through 115 were rejected under 35 USC §112, first paragraph, for assertedly failing to comply with the written description requirement. It was the examiner's position that the claims are "drawn to a method of treatment comprising the administration of an agent, wherein the agent is described in terms of its function." [Office Action at p. 2] To purportedly support this rejection, the examiner relied on the Federal Circuit's decision in *UC v. Lilly* requiring satisfaction of the written description requirement for a claimed genus to include "a representative number of species by actual reduction to practice..., reduction to drawings..., or by disclosure of relevant, identifying characteristics, i.e., structure or other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the claimed genus." [Office Action at p. 2] The examiner also relied on the decision in *Rochester v. Searle*, stating "it is only necessary that the patent set forth enough detail to allow a person of ordinary skill in the art to understand what is claimed and to recognize that the inventor invented what is claimed." [Office Action at p. 2]

The applicants respectfully traverse the rejection. First, the decision in *UC v. Lilly* is off point with the facts relating to the instantly claimed subject matter. Second, the decision in *Rochester v. Searle* actually supports the position that the specification satisfies the written description requirement of section 112. Finally, even if the decision in *UC v. Lilly* were on point, the applicants have provided the requisite number of species to describe the claims genus.

The subject matter of the rejected claims relates to methods of treatment using compounds that were known to exist in the art.[1] The specification makes this point unambiguously clear in the disclosure of specific compounds (and derivatives thereof) which meet the "functional definition" of the agent recited in claim 44 in its ability to bind copper and form an agent-copper-protein complex. See, for example, p. 5, line 24, through p. 6, line 11; p. 28, line 2, through p. 32, line 28.

The rejected subject matter at issue in *UC v. Lilly,* however, was a genus of polynucleotides encoding mammalian insulin, and the specification purportedly supported the claimed subject matter with the disclosure of a single polynucleotide encoding rodent insulin. Prior to disclosure of the rodent polynucleotide, no mammalian polynucleotide encoding insulin was known in the art. Therein lies the distinction between the facts in *UC v. Lilly* and the present application; in *Lilly* a genus of previously unknown compounds was being claimed, while here, use of known compounds is being claimed. The Federal Circuit has recently acknowledged this distinction as being significant.

In *Capon v. Eshhar*, Docket No. 03-1480, -1481, decided August 12, 2005 (a copy of which is attached hereto), the Federal Circuit vacated and remanded the decision of the Board of Patent Appeals and Interferences ("the Board") holding all claims of both parties corresponding to the count in Interference No. 103,887 unpatentable for lack of written description. The subject matter of the count related to "chimeric genes" comprising, *inter alia*, a gene segment encoding a single chain antibody Fv domain and a gene segment encoding a transmembrane domain. The Board based its holding of lack of written

[1] The applicants note, however, that compounds identified or produced at some future date which possess the required functional capacity will also fall within the scope of the claims.

description for failure to satisfy the requirements set out in *UC v. Lilly.* The Federal Circuit however, saw things differently.

The Court stated,

> The written description requirement states that the patentee must describe the invention; it does not state that every invention must be described in the same way. As each field evolves, the balance also evolves between what is known and what is added by each invention. Both Eshhar and Capon explain that this invention does not concern the discovery of gene function or structure, as in Lilly. The chimeric genes here at issue are prepared from known DNA sequences of known function.

The same distinction can be made between the subject matter in *UC v. Lilly* and the instantly claimed subject matter. No new products are disclosed or recited in the presently rejected claims; the claims simply address new uses. Thus, the holding and requirements as set out in *UC v. Lilly* is no more appropriate here as it was in *Capon.*

Regarding the examiner's reliance on *Rochester*, the applicants again submit that the facts therein are wholly distinguishable from those in the instant matter. In *Rochester*, claims directed to methods of selectively inhibiting PGHS-2 enzyme activity were found to lack written descriptive support because the specification did not disclose a single compound which could be used in the methods to achieve the recited result. That finding cannot be made in the present application. As noted above, the instant specification unambiguously discloses a number of compounds (and derivatives thereof) which are described to be effective in carrying out the method of claim 44. Again, see, for example, p. 5, line 24, through p. 6, line 11; p. 28, line 2, through p. 32, line 28. Thus, the examiner's reliance on *Rochester* is misplaced.

The discussion above makes evident that the examiner has applied an improper legal basis to asserted that the subject matter of the rejected claims lacks written descriptive

support in the present application, and for the reasons set out above, the rejection of claims under section 112 must be withdrawn.

As a final note, however, the applicants assume *arguendo* the examiner's reliance on *UC v. Lilly* is appropriate to the extent that a reasonable number of species are required to support a claimed genus. Again as noted above, the present specification discloses a number of specific compounds (i.e., agents), and derivatives thereof, that fall within the scope of the recited functional definition requiring copper binding and the ability to form a copper-agent-protein complex. Once again, see, for example, p. 5, line 24, through p. 6, line 11; p. 28, line 2, through p. 32, line 28. The number of these disclosed compounds is believed to be more than "representative" and thus, even if the *UC v. Lilly* analysis were proper, the present specification would satisfy the written description requirement therein.

The second rejection of claims under 35 USC §112, first paragraph

Claim 44 and 80 through 115 were also rejected under 35 USC 112, first paragraph, for assertedly lacking an enabling disclosure in the specification. The examiner asserted that

> any methods for making agents other than thiomolybdate derivatives are not enabled due to lack of written description. This is addressed above. [Office Action. p. 6]

The examiner also asserted that a post-filing publication co-authored by a present inventor indicated that it was "unlikely" that tetrathiomolybdate (TM) will be effective in macular degeneration, and that the authors had "no basis for prediction of whether TM will be useful in other diseases where neovascularization is a factor, such as psoriasis and rheumatoid arthritis." [Office Action, p. 6, citations omitted] The examiner also relied on a second later-published reference by Elner, et al., for purportedly disclosing the "TM significantly reduced neovascularization *only if used before its onset.*" [Emphasis added by the examiner.] The

examiner thus concluded that treatment of the recited diseases was not enabled at the time of filing.

With regard to the first part of this rejection, that "any methods for making agents other than thiomolybdate derivatives are not enabled due to lack of written description," the applicants note that the claims are not directed to any methods of making agents useful in the recited methods of treatment. Thus, whether the specification teaches how to "make" agents other than thiomolybdate derivative is irrelevant to the question of if making and using the claimed method is enabled. The applicants exemplified useful agents with the discussion of various thiomolybdate compounds, thereby teaching how to make and use the method as claimed.

Furthermore, the applicants note that the specification also teaches use of other copper-chelating agents, beginning at page 35, line 6, which the worker of ordinary skill in the art would understand could be useful alone or in modified forms to achieve the desired reduction of free copper as provided by the thiomolybdate compounds.

Regarding the examiner's reliance on the two cited references, it is first submitted that the methods of the invention provide a reduction in free copper, and it is disclosed in the specification (for example at page 18, line 23, to page 19, line 27) that free copper is required for angiogenesis, and in particular, for the action of angiogentic mediators. See, in particular, p. 18, lines 23 through 25. The application unambiguously demonstrates that methods of the invention reduce free copper. See p. 90, section 4. Thus, one of ordinary skill in the art at the time the application was filed would have predicted that a method that would reduce free copper would have a detrimental effect on any and all biological processes which require free copper, such as angiogenesis. The same worker of ordinary skill would have predicted that angiogenesis, or neovascularization, would be one of these processes affected in a negative

manner upon reduction of free copper since it was known that angiogenesis required free copper. Thus, there would have been, at the time the application was filed, a sound scientific basis for the worker of ordinary skill to have predicted this result, and the specification taught how to bring it about.

Turning now to comments in the Brewer reference on which the examiner relies, it is submitted that the authors only suggest that is "seems unlikely" that TM will be effective in macular degeneration "based on one pilot clinical trial." The paper does not provide the raw results of this trial, and thus there is no way to evaluate the clinical results in terms of whether TM treatment provided absolutely no effect on macular degeneration or provided an effect that was insignificant to the point that clinical application would be unfeasible from an economic standpoint. The same is true for the cited passage in the Elner reference; one cannot conclude that there was absolutely no effect on the condition following administration of the disclosed agent.

Despite this uncertainty, the examiner appears to believe that the later-filed references demonstrate that the method as claimed had absolutely no therapeutic benefit. Yet, on the balance of probabilities, the underlying factual basis for predicting the methods would work argue against the possibility that absolutely no positive effect was achieved. It is simply improbably that reducing free copper would have absolutely no effect on a biological process which requires free copper.

Inasmuch as this rejection relates more closely to an asserted lack of utility with respect to various disease states recited in the claims, the applicants note that the MPEP states at section 2107.01,

> Office personnel should not construe 35 U.S.C. 101, under the logic of "practical" utility or otherwise, to require that an applicant demonstrate that a therapeutic agent based on a claimed invention is a safe or **fully effective** drug for humans.

> See, e.g., In re Sichert, 566 F.2d 1154, 196 USPQ 209 (CCPA 1977); In re Hartop, 311 F.2d 249, 135 USPQ 419 (CCPA 1962); In re Anthony, 414 F.2d 1383, 162 USPQ 594 (CCPA 1969); In re Watson, 517 F.2d 465, 186 USPQ 11 (CCPA 1975). [Emphasis added.]

Thus, there is no requirement that a method be fully effective in therapeutic treatment. Presumably then, any effect to any degree in the desired direction (i.e., up- or down-regulation) would indicate that the treatment method worked. Whether the method is safe or economically practicable is not relevant to patentability.

Accordingly the applicants submit that the references on which the examiner relies to assert a lack of enablement do not provide conclusive support for the position that certain conditions are completely unaffected by the claimed methods. Absent evidence that absolutely no positive effect is achieved, the applicants submit that the rejection cannot be sustained and must be withdrawn.

The third rejection of claims under 35 USC §112, first paragraph

The examiner also rejected claims 116 through 122 under section 112, first paragraph, stating that the claims, while appearing to be enabled for treatment of cancer but not to other recited diseases. The examiner listed the factors set out in *Wands* for which consideration is given in a determination of undue experimentation and stated (i) no data for disease other than cancer has been disclosed, (ii) based on the references discussed above, treatment of non-cancer diseases related to aberrant vascularization have been negative, (iii) the level of skill in the art is likely to be high, and (iv) predictability in the art appears to be low. Thus the examiner concluded practice of the full scope of the invention would require undue experimentation. The applicants respectfully disagree.

The data disclosed in the specification with respect to treatment of cancer shows that, as predicted, the method of the invention reduces free copper. As discussed above, the specification shows that copper is required for angiogenesis and in particular for factors required in the angiogentic process. Thus, the worker of ordinary skill in the art would find it likely that a condition arising from aberrant angiogenesis would be alleviated, at least to some degree, with a treatment regimen than reduces free copper as required for the angiogenesis to progress. With knowledge of the data in the specification showing that this positive result was achieved in treatment of cancer, the same worker of ordinary skill would be even more likely to predict a similar result for treating other conditions. As discussed above, the extent to which a result is achieved is irrelevant, especially since the claims recite a method of "treatment," not a method of "curing."

As discussed above, the references on which the examiner relies do not unambiguously disclose that treatment with a method of the invention has absolutely no effect on various conditions mentioned in these references. The discussion addressing another aspect of the rejection under 112, first paragraph, presented immediately above is incorporated in its entirety in response to the rejection in this section.

In consideration of these factors, together with the high level of skill in the art, which would include well-accepted and routinely-practiced models for each of the variously recited disease states, the applicants submit that nothing more than routine experimentation would be required to carry out the full scope of the invention as claimed. Accordingly, the applicants submit that the rejection may properly be withdrawn.

The rejection of claims under 35 USC §§102(a) and 103(a)

The examiner rejected claims 116, 117 and 120 under section 102(a) as being directed to subject matter assertedly anticipated, or in the alternative directed to subject matter rendered obvious, by the disclosure of Merajver, *et al.*, Proc. Angiogen. Cancer (1998). The examiner stated that submission of a copy of a *Katz* declaration provided in the parent application would remove this reference from consideration. Accordingly, with submission of a copy of this declaration, the rejections are obviated.

The rejection of claims for double patenting

Claims 44, 80, 83-85, 104, 106, 107, and 116 through 122 were rejected under the judicially created doctrine of obviousness-type double patenting as being rendered obvious by the subject matter of claims 43 through 48, and 57 of US Patent No. 6,703,050. The same rejection was made with respect to claims 116, 117, 119 and 122 over claims 3, 15 through 18 and 36 though 42 of the same patent.

The applicants acknowledge the rejections and will address the issue once allowable subject matter has been found in the present application.

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Respectfully submitted,

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